



## **Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States**

Downloaded from <https://aidsinfo.nih.gov/guidelines> on 8/31/2020

Visit the *AIDSinfo* website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <https://aidsinfo.nih.gov/e-news>.

### Panel's Recommendations

- All pregnant women with HIV should be screened during the current pregnancy for hepatitis C virus (HCV) infection unless they are known to have HCV/HIV coinfection (**AIII**).
- HCV screening should be repeated later in pregnancy in women who initially screen negative for HCV but who have persistent or new risk factors for HCV (e.g., new or ongoing injection or intranasal substance use) (**AIII**).
- All pregnant women with HIV should also be tested for hepatitis B virus (HBV) infection, unless they are known to have HBV/HIV coinfection or if they have serologic documentation of HBV immunity (see [Hepatitis B Virus/HIV Coinfection](#)).
- Women with HCV infection who have not already received the hepatitis A virus (HAV) vaccine series should be screened for immunity to HAV (**AIII**). If they screen negative for HAV antibodies (IgG or IgG plus IgM), they should receive the HAV vaccine series (**AIII**).
- All pregnant women with HIV and/or HCV who screen negative for HBV infection (i.e., HBV surface antigen negative, HBV core antibody negative, and HBV surface antibody negative) or who lack HBV immunity (i.e., HBV surface antibody negative) should receive the HBV vaccine series (**AII**).
- Currently, treatment of HCV during pregnancy **is not recommended** due to the lack of safety data on the use of HCV direct-acting antiviral medications in pregnant women. When considering initiating HCV treatment in a pregnant woman with HIV coinfection, consultation with an expert in HIV and HCV is strongly recommended (**AIII**).
- Recommendations for antiretroviral therapy (ART) during pregnancy are the same for all women living with HIV, whether they have HCV or not (**AIII**).
- Pregnant women with HCV/HIV coinfection who are receiving ART should be counseled about the signs and symptoms of liver toxicity, and hepatic transaminases should be assessed 1 month following initiation of ART and at least every 3 months thereafter during pregnancy (**BIII**).
- Decisions concerning the mode of infant delivery in pregnant women with HCV/HIV coinfection should be based on standard obstetric and HIV-related indications alone; HCV coinfection does not necessitate cesarean delivery when not otherwise indicated (see [Transmission and Mode of Delivery](#)) (**AIII**).
- Infants born to women with HCV/HIV coinfection should be evaluated for HCV infection (**AIII**). Decisions regarding the specific type of assays to use for HCV screening in children and the timing of those assays should be made after consultation with an expert in pediatric HCV infection (**AIII**).

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

For additional information on hepatitis C virus (HCV) and HIV, see [Hepatitis C Virus](#) in the [Pediatric Opportunistic Infection Guidelines](#), [Hepatitis C Virus/HIV Coinfection](#) in the [Adult and Adolescent Antiretroviral Guidelines](#), and [Hepatitis C Virus Infection](#) in the [Adult and Adolescent Opportunistic Infection Guidelines](#). The American Association for the Study of Liver Diseases, the Infectious Diseases Society of America, and the International Antiviral Society-USA maintain updated information about treating patients with HCV/HIV coinfection. The guidelines are available online at [HCVguidelines.org](http://HCVguidelines.org). The management of HCV/HIV coinfection in pregnancy is complex, and none of the approved HCV direct-acting antivirals (DAAs) have yet been fully evaluated in pregnant women; thus, consultation with an expert in HIV and HCV infection **is strongly recommended** when managing HCV during pregnancy.

### Screening and Vaccination

All pregnant women living with HIV should be screened at entry into general HIV care and during each pregnancy for:

- Hepatitis B virus (HBV), unless they are known to have HBV/HIV coinfection or they have serologic documentation of HBV immunity, *and*
- HCV infection, unless they are known to have HCV/HIV coinfection.

Among women with HIV, the observed risks for HCV infection were 2% to 12% in European cohorts of pregnant women with HIV<sup>1</sup> and 3.8% among women with HIV in New York State.<sup>2</sup> Although data about secular trends in HCV risk among women living with HIV are limited in the United States, the prevalence of HCV among women of childbearing age and children aged <2 years in the general population has increased substantially in recent years, **due in part to the ongoing opioid epidemic in the United States.**<sup>3-9</sup>

**The Society for Maternal-Fetal Medicine and the American College of Obstetricians and Gynecologists recommend repeating HCV testing later in pregnancy for women who initially screen negative for HCV but who have persistent risk factors for HCV or who develop new risk factors for HCV infection (e.g., new or ongoing use of injected or intranasal substance use).**<sup>10</sup> The male partners of all women with HCV/HIV coinfection should be referred for both HIV and hepatitis counseling and testing to prevent the sexual transmission of HIV and HCV; however, HCV is infrequently transmitted via heterosexual sex. People who do not share injection equipment have a very low risk of horizontal transmission of HCV. Partners who do not have HIV infection should be counseled about the potential benefits and risks of starting oral pre-exposure prophylaxis to prevent HIV acquisition (see [Preconception Counseling and Care for Women of Childbearing Age Living with HIV](#)).

Newly available DAAs have dramatically improved HCV therapy; it is now possible to cure HCV infection in most patients.<sup>11</sup> Current HCV treatment guidelines recommend therapy for nearly all patients with HCV infection.<sup>11</sup> The management of HCV/HIV coinfection during pregnancy is complex, however. A Phase 1 study is now evaluating the safety and pharmacokinetics (PKs) of ledipasvir/sofosbuvir in pregnancy; early data from this study were recently presented at a conference.<sup>12</sup> Ribavirin is also contraindicated in pregnancy, though it is no longer commonly needed for the treatment of HCV.<sup>13</sup> When considering HCV treatment for a pregnant person, consultation with an expert in HIV and HCV is strongly recommended. In addition, the risk of perinatal HCV transmission is much lower than the risk of perinatal HIV transmission, and some children will clear HCV infection spontaneously;<sup>5,14,15</sup> therefore, treating HCV during pregnancy presents different risks and benefits than treating HIV during pregnancy.

The primary reasons for HCV testing during pregnancy are:

- To identify women with HCV/HIV coinfection at a time when they are engaged with the health care system, so that HCV treatment can be offered after delivery (ideally before a subsequent pregnancy);
- To monitor for HCV-related hepatotoxicity, which has been associated with the use of antiretroviral (ARV) drugs in women with HCV/HIV coinfection;<sup>16</sup>
- To monitor for preterm birth, which has been associated with HIV/HCV coinfection in pregnant women;<sup>1,8,17,18</sup>
- To ensure vaccination against other viral hepatitis infections (hepatitis A virus [HAV] and HBV) when needed; *and*
- To ensure appropriate follow-up and evaluation of infants who were exposed to HCV.

Screening for chronic HCV infection using a sensitive immunoassay for HCV antibodies is recommended for all individuals with HIV, including those who are pregnant. False-negative anti-HCV immunoassay results can occur in individuals with HIV, but it is uncommon with the more sensitive immunoassays. If HCV infection is suspected despite a negative HCV antibody screen, **a commercially available diagnostic quantitative plasma HCV RNA assay** can be performed.<sup>19,20</sup> Individuals who have a positive HCV antibody test should undergo confirmatory testing for **HCV RNA with this quantitative assay**. Many laboratories now perform reflex RNA testing for individuals who test positive for HCV antibodies. Pregnant women should also be tested for HCV RNA when they have indeterminate or negative serologic test results for HCV but are suspected of having HCV infection because of elevated aminotransaminase levels or risk factors such as a history of injection drug use.<sup>21</sup>

Because of the added risk of hepatic decompensation from acute infection with any viral hepatitis, women with HCV infection should also be screened for both HAV and HBV. Women with chronic HCV infection who have not already received the HAV vaccine series should be screened for immunity to HAV (either IgG alone or IgG and IgM together). If they screen negative for HAV antibodies, they should receive the HAV vaccine

series. In women with CD4 T lymphocyte (CD4) cell counts  $<200$  cells/mm<sup>3</sup>, antibody responses to the HAV vaccine should be assessed 1 month after the patient completes the vaccination series; those who are HAV antibody IgG negative should be revaccinated when the CD4 count is  $>200$  cells/mm<sup>3</sup>.<sup>22</sup> Women with HCV/HIV coinfection who screen negative for HBV (i.e., they are hepatitis B surface antigen [HBsAg] negative, hepatitis B core antibody negative, and hepatitis B surface antibody negative [HBsAb]) **or who lack HBV immunity (i.e., they are HBV surface antibody negative)** should receive the HBV vaccine series. Women with HCV/HIV coinfection who are HBsAb negative despite receiving the HBV vaccine series may benefit from revaccination (see [Hepatitis B Virus/HIV Coinfection](#)).<sup>23</sup> The hepatitis B vaccination poses no apparent risk to developing fetuses, as current vaccines contain noninfectious HBsAg.<sup>24</sup>

### ***Impact of HCV/HIV Coinfection on Progression and Perinatal Transmission of Both Viruses***

Although the HCV viral load appears to peak in the third trimester, pregnancy does not appear to influence the course of HCV infection clinically. Women with chronic HCV generally do well during pregnancy, provided that they have not progressed to decompensated cirrhosis.<sup>25,26</sup>

### **Hepatitis C Virus Transmission**

Approximately six of every 100 infants born to women with HCV acquire HCV infection.<sup>20</sup> In most studies of women with HCV/HIV coinfection who are not receiving treatment for either infection, the incidence of perinatal HCV transmission is approximately two-fold higher among women with HCV/HIV coinfection (10% to 20% transmission risk) than among women with HCV mono-infection.<sup>27-30</sup> These higher transmission rates are likely related to the higher levels of HCV viremia observed in patients with HCV/HIV coinfection and/or other HIV-related impacts on HCV disease activity.<sup>18,31</sup> However, early and sustained control of HIV viremia with antiretroviral therapy (ART) may reduce the risk of HCV transmission to infants.<sup>26,32,33</sup> A European study of perinatal HCV transmission found that the use of effective ART for HIV was associated with a strong trend toward reduced rates of HCV transmission (odds ratio [OR] 0.26; 95% confidence interval [CI], 0.07–1.01).<sup>32</sup> In an Italian cohort, HCV transmission occurred in 9% of infants born to women with HCV/HIV coinfection, most of whom were on ART. No HCV transmissions occurred in infants born to women with HCV viral loads of  $<5$  log IU/mL.<sup>18</sup>

### **HIV Transmission**

In the absence of ART, maternal HCV/HIV coinfection also may increase the risk of perinatal HIV transmission.<sup>34,35</sup> The risk of perinatal HIV transmission can likely be reduced in pregnant women with HCV/HIV coinfection by following the standard recommendations for ART for all women with HIV.

### ***Impact of Hepatitis C Virus on HIV Management***

Data are limited on the optimal management of pregnant women with HCV/HIV coinfection. Recommendations on the use of ART during pregnancy for treating HIV and preventing perinatal HIV transmission are the same for women who have HCV/HIV coinfection as for those with HIV mono-infection (see [General Principles Regarding Use of Antiretroviral Drugs during Pregnancy](#)). In one Canadian study, HCV/HIV coinfection was associated with an increased risk of HIV viral rebound among women who were on previously effective ART. Although the authors suggest that additional factors (e.g., adherence) may have varied between the groups, these findings support the need to follow recommendations for HIV RNA monitoring during pregnancy.<sup>36</sup>

### ***Hepatitis C Virus-Specific Therapy in Pregnancy***

All currently available DAAs lack sufficient safety data to be recommended for use during pregnancy. In the past, most anti-HCV therapy included both interferon and ribavirin. Interferons are not recommended for use in pregnancy because they are abortifacient at high doses in monkeys and have direct antigrowth and antiproliferative effects.<sup>37</sup> Some DAA regimens are approved for use with ribavirin in specific nonpregnant populations, due to the suboptimal treatment responses observed with the use of DAAs alone. Any

treatment regimens that include ribavirin are **contraindicated** in pregnant women due to the teratogenic and embryocidal effects observed in all animal species exposed to ribavirin. Ribavirin-associated defects in animals include limb abnormalities, craniofacial defects, anencephaly, and anophthalmia. Pregnancies that occur in women taking ribavirin should be reported to the [Ribavirin Pregnancy Registry](#) (online or by phone at 1-800-593-2214).

There are many interferon-free DAA regimens that have been approved for the treatment of HCV. When determining the optimal regimen for an individual patient, clinicians must consider many factors, including HCV genotype, prior treatment experience, and stage of liver disease (e.g., compensated or decompensated cirrhosis). There are four main classes of DAAs:<sup>11,38</sup>

- NS5A inhibitors: daclatasvir, elbasvir, ledipasvir, ombitasvir, pibrentasvir, velpatasvir
- NS5B nucleoside polymerase inhibitors: sofosbuvir
- NS5B non-nucleoside polymerase inhibitors: dasabuvir
- NS3/4A protease inhibitors (PIs): glecaprevir, grazoprevir, paritaprevir, simeprevir, voxilaprevir

DAAs are not yet recommended for use in pregnancy because of the lack of PK and safety data; [one small PK study](#) that is investigating the use of ledipasvir/sofosbuvir in pregnant women with HCV alone is ongoing.<sup>12</sup> In addition, potential drug interactions exist between these newer anti-HCV drugs and ARV drugs that may produce clinically significant changes in serum levels of both ARV drugs and anti-HCV medications. For detailed information on the interactions between ARV drugs and anti-HCV drugs, see the [Adult and Adolescent Antiretroviral Guidelines](#), the [Adult and Adolescent Opportunistic Infection Guidelines](#), [HCVGuidelines.org](#), and the [HEP Drug Interaction Checker](#).

### ***Monitoring Women with HCV/HIV Coinfection During Pregnancy***

Hepatic enzyme levels can increase after ART is initiated in women with HCV/HIV coinfection—particularly in those with low CD4 counts at treatment initiation—as a result of an immune-mediated flare in HCV disease triggered by immune reconstitution with ART. In patients with HIV, HCV infection may increase the hepatotoxic risk of certain ARV agents, specifically PIs and nevirapine. HCV mono-infection may increase the risk of intrahepatic cholestasis of pregnancy;<sup>39</sup> **this risk is also higher among women with HCV/HIV coinfection than among women with HIV infection alone.**<sup>1</sup> Pregnant women with HCV/HIV coinfection should be counseled about the signs and symptoms of liver toxicity, and transaminase levels should be assessed 1 month after initiating ART and then every 3 months thereafter. If hepatic toxicity occurs, a clinician may need to consider initiating a less hepatotoxic drug regimen, and, if clinical symptoms or significant elevations of transaminases occur, drugs may need to be temporarily discontinued. Differentiating between drug toxicity and a flare of HCV disease that is associated with immune reconstitution can be difficult; therefore, consulting an expert in HCV/HIV coinfection is strongly recommended.

Rates of preterm delivery are also high among women with HCV/HIV coinfection. In an Italian cohort of mostly ART-treated women with HCV/HIV coinfection, preterm delivery occurred in 41% of women overall. The rate of preterm delivery was 29% among women with HCV RNA <5 log IU/mL and 43% among women with HCV RNA >5 log IU/mL; the difference in rates of preterm delivery was not statistically significant between the two groups. Women with preterm delivery had significantly higher levels of HCV RNA than those who delivered at term.<sup>18</sup> **In a population-based retrospective cohort of 87,924 pregnant women in the United States who delivered between 2006 and 2014, infants born to women with HCV (n = 1,043; 1.2%) were more likely to be preterm (defined as <37 weeks gestation) than those born to women without HCV (22% vs. 10%, *P* < 0.01). Infants born to women with HCV were also more likely to have low birth weights (defined as weighing <2,500 g) than those born to women without HCV (23% vs. 8%, *P* < 0.01).**<sup>8</sup>

HCV infection in pregnancy may also be associated with increased risks for gestational diabetes, small-for-gestational-age infants, and low birth weight infants.<sup>5,40</sup> **A study of 4,236 pregnant women with HIV reported a higher risk of preterm delivery in women with HCV coinfection (OR 3.0; 95% CI, 1.6–5.7) than in women with HIV alone.**<sup>1</sup> Although currently no obstetric guidelines suggest that women with HCV infection should



be monitored more frequently for diabetes or for fetal growth,<sup>41</sup> knowledge of these increased risks may inform clinical care.<sup>10</sup>

## Mode of Delivery

The majority of studies of scheduled cesarean delivery in women with HCV infection (with or without HIV coinfection) have found that the procedure does not reduce the risk of perinatal HCV transmission.<sup>32,42-44</sup> Thus, the general recommendations for mode of delivery are the same for women with HCV/HIV coinfection as for those with HIV infection alone (see [Transmission and Mode of Delivery](#)).

## Evaluation of Infants Exposed to Hepatitis C Virus

Infants born to women with HCV/HIV coinfection should be assessed for chronic HCV infection. An HCV antibody test should be performed after age 18 months, when the maternal anti-HCV antibody level has waned.<sup>45</sup> Sensitivity of HCV RNA testing is low at birth, and viremia can be intermittent or infection may resolve spontaneously; thus, HCV RNA testing should not be performed before age 2 months, and a single negative test is not conclusive evidence of lack of infection.<sup>46</sup> Uptake of HCV testing is very low for infants who were exposed to HCV; therefore, it is important for providers to counsel women about the need for pediatric follow-up and testing during the first few years of life.<sup>8,47-49</sup> The [Pediatric Opportunistic Infection Guidelines](#) provide further details about the diagnostic evaluation of infants who were exposed to HCV.

## References

1. Benhammou V, Tubiana R, Matheron S, et al. HBV or HCV coinfection in HIV-1-infected pregnant women in France: prevalence and pregnancy outcomes. *J Acquir Immune Defic Syndr*. 2018;77(5):439-450. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29287028>.
2. Ghazaryan L, Smith L, Parker M, et al. Hepatitis C seroprevalence among HIV-infected childbearing women in New York state in 2006. *Matern Child Health J*. 2016;20(3):550-555. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26520159>.
3. Koneru A, Nelson N, Hariri S, et al. Increased hepatitis C virus (HCV) detection in women of childbearing age and potential risk for vertical transmission - United States and Kentucky, 2011-2014. *MMWR Morb Mortal Wkly Rep*. 2016;65(28):705-710. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27442053>.
4. Ly KN, Jiles RB, Teshale EH, Foster MA, Pesano RL, Holmberg SD. Hepatitis C virus infection among reproductive-aged women and children in the United States, 2006 to 2014. *Ann Intern Med*. 2017;166(11):775-782. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28492929>.
5. Barritt AS, 4th, Jhaveri R. Treatment of hepatitis C during pregnancy—weighing the risks and benefits in contrast to HIV. *Curr HIV/AIDS Rep*. 2018;15(2):155-161. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29470782>.
6. Salemi JL, Spooner KK, Mejia de Grubb MC, Aggarwal A, Matas JL, Salihu HM. National trends of hepatitis B and C during pregnancy across sociodemographic, behavioral, and clinical factors, United States, 1998-2011. *J Med Virol*. 2017;89(6):1025-1032. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27805270>.
7. Patrick SW, Bauer AM, Warren MD, Jones TF, Wester C. Hepatitis C virus infection among women giving birth - Tennessee and United States, 2009-2014. *MMWR Morb Mortal Wkly Rep*. 2017;66(18):470-473. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28493860>.
8. Chappell CA, Hillier SL, Crowe D, Meyn LA, Bogen DL, Krans EE. Hepatitis C virus screening among children exposed during pregnancy. *Pediatrics*. 2018;141(6). Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29720535>.
9. Schillie SF, Canary L, Koneru A, et al. Hepatitis C virus in women of childbearing age, pregnant women, and children. *Am J Prev Med*. 2018;55(5):633-641. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30342628>.
10. Society for Maternal-Fetal Medicine, Hughes BL, Page CM, Kuller JA. Hepatitis C in pregnancy: screening, treatment, and management. *Am J Obstet Gynecol*. 2017;217(5):B2-B12. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28782502>.
11. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. HCV guidance: recommendations for testing, managing, and treating hepatitis C. 2017. Available at: <http://hcvguidelines.org/>.

12. Chappell CA, Kranss E, Bunge K, et al. A phase 1 study of ledipasvir/sofosbuvir in pregnant women with hepatitis C virus. Abstract 87. Presented at: Conference on Retroviruses and Opportunistic Infections. 2019. Seattle, WA. Available at: <http://www.croiconference.org/sessions/phase-1-study-ledipasvirsofosbuvir-pregnant-women-hepatitis-c-virus>.
13. Spera AM, Eldin TK, Tosone G, Orlando R. Antiviral therapy for hepatitis C: has anything changed for pregnant/lactating women? *World J Hepatol*. 2016;8(12):557-565. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27134703>.
14. Mack CL, Gonzalez-Peralta RP, Gupta N, et al. NASPGHAN practice guidelines: Diagnosis and management of hepatitis C infection in infants, children, and adolescents. *J Pediatr Gastroenterol Nutr*. 2012;54(6):838-855. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22487950>.
15. Bernstein HB, Dunkelberg JC, Leslie KK. Hepatitis C in pregnancy in the era of direct-acting antiviral treatment: potential benefits of universal screening and antepartum therapy. *Clin Obstet Gynecol*. 2018;61(1):146-156. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29351151>.
16. Sibiude J, Warszawski J, Tubiana R, et al. High risk of liver enzyme elevation in pregnant women receiving protease inhibitors. Presented at: Conference on Retroviruses and Opportunistic Infections. 2016. Boston, MA.
17. Huang QT, Huang Q, Zhong M, et al. Chronic hepatitis C virus infection is associated with increased risk of preterm birth: a meta-analysis of observational studies. *J Viral Hepat*. 2015;22(12):1033-1042. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26081198>.
18. Baroncelli S, Pirillo MF, Amici R, et al. HCV-HIV coinfecting pregnant women: data from a multicentre study in Italy. *Infection*. 2016;44(2):235-242. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26507133>.
19. Alter MJ, Kuhnert WL, Finelli L, Centers for Disease C, Prevention. Guidelines for laboratory testing and result reporting of antibody to hepatitis C virus. Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 2003;52(RR-3):1-13, 15; quiz CE11-14. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12585742>.
20. Centers for Disease Control and Prevention. Hepatitis C questions and answers for health professionals. 2019. Available at: <https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm>.
21. Centers for Disease Control and Prevention. Viral hepatitis - hepatitis C information. 2019. Available at: <http://www.cdc.gov/hepatitis/hcv/>.
22. Panel on Antiretroviral Guidelines for Adults and Adolescents. Hepatitis B virus/HIV coinfection. 2018. Available at: <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/25/hbv-hiv>.
23. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents—Hepatitis C Virus Infection. 2018. Available at: <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/26/hcv-hiv>.
24. Centers for Disease Control and Prevention. Guidelines for vaccinating pregnant women. 2017. Available at: <https://www.cdc.gov/vaccines/pregnancy/hcp/guidelines.html>.
25. Sookoian S. Effect of pregnancy on pre-existing liver disease: chronic viral hepatitis. *Ann Hepatol*. 2006;5(3):190-197. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17060881>.
26. Benova L, Mohamoud YA, Calvert C, Abu-Raddad LJ. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. *Clin Infect Dis*. 2014;59(6):765-773. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24928290>.
27. Tovo PA, Palomba E, Ferraris G, et al. Increased risk of maternal-infant hepatitis C virus transmission for women coinfecting with human immunodeficiency virus type 1. Italian Study Group for HCV Infection in Children. *Clin Infect Dis*. 1997;25(5):1121-1124. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9402369>.
28. Gibb DM, Goodall RL, Dunn DT, et al. Mother-to-child transmission of hepatitis C virus: evidence for preventable peripartum transmission. *Lancet*. 2000;356(9233):904-907. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11036896>.
29. Mast EE, Hwang LY, Seto DS, et al. Risk factors for perinatal transmission of hepatitis C virus (HCV) and the natural history of HCV infection acquired in infancy. *J Infect Dis*. 2005;192(11):1880-1889. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16267758>.
30. Alter MJ. Epidemiology of viral hepatitis and HIV co-infection. *J Hepatol*. 2006;44(1 Suppl):S6-9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16352363>.
31. Polis CB, Shah SN, Johnson KE, Gupta A. Impact of maternal HIV coinfection on the vertical transmission of hepatitis C

- virus: a meta-analysis. *Clin Infect Dis*. 2007;44(8):1123-1131. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17366462>.
32. European Paediatric Hepatitis C Virus Network. A significant sex--but not elective cesarean section--effect on mother-to-child transmission of hepatitis C virus infection. *J Infect Dis*. 2005;192(11):1872-1879. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16267757>.
  33. Checa Cabo CA, Stoszek SJ, Quarleri J, et al. Mother-to-child transmission of hepatitis C virus (HCV) among HIV/HCV-coinfected women. *J Ped Infect Dis*. 2013;2(2):126-135. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26199724>.
  34. Hershow RC, Riester KA, Lew J, et al. Increased vertical transmission of human immunodeficiency virus from hepatitis C virus-coinfected mothers. Women and infants transmission study. *J Infect Dis*. 1997;176(2):414-420. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9237706>.
  35. England K, Thorne C, Newell ML. Vertically acquired paediatric coinfection with HIV and hepatitis C virus. *Lancet Infect Dis*. 2006;6(2):83-90. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16439328>.
  36. Boucoiran I, Albert AYK, Tulloch K, et al. Human immunodeficiency virus viral load rebound near delivery in previously suppressed, combination antiretroviral therapy-treated pregnant women. *Obstet Gynecol*. 2017;130(3):497-501. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28796673>.
  37. Boskovic R, Wide R, Wolpin J, Bauer DJ, Koren G. The reproductive effects of beta interferon therapy in pregnancy: a longitudinal cohort. *Neurology*. 2005;65(6):807-811. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16186517>.
  38. Elbasvir/grazoprevir (Zepatier) [package insert]. Food and Drug Administration. 2016. Available at: [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/208261Orig1s0001bl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208261Orig1s0001bl.pdf).
  39. Wijarnpreecha K, Thongprayoon C, Sanguankeo A, Upala S, Ungprasert P, Cheungpasitporn W. Hepatitis C infection and intrahepatic cholestasis of pregnancy: A systematic review and meta-analysis. *Clin Res Hepatol Gastroenterol*. 2017;41(1):39-45. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27542514>.
  40. Pergam SA, Wang CC, Gardella CM, Sandison TG, Phipps WT, Hawes SE. Pregnancy complications associated with hepatitis C: data from a 2003-2005 Washington state birth cohort. *Am J Obstet Gynecol*. 2008;199(1):38 e31-39. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18486089>.
  41. American College of Obstetricians Gynecologists. ACOG practice bulletin No. 86: viral hepatitis in pregnancy. *Obstet Gynecol*. 2007;110(4):941-956. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17906043>.
  42. Ghamar Chehreh ME, Tabatabaei SV, Khazanehdari S, Alavian SM. Effect of cesarean section on the risk of perinatal transmission of hepatitis C virus from HCV-RNA+/HIV- mothers: a meta-analysis. *Arch Gynecol Obstet*. 2011;283(2):255-260. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20652289>.
  43. Marine-Barjoan E, Berrebi A, Giordanengo V, et al. HCV/HIV co-infection, HCV viral load and mode of delivery: risk factors for mother-to-child transmission of hepatitis C virus? *AIDS*. 2007;21(13):1811-1815. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17690581>.
  44. McMenamin MB, Jackson AD, Lambert J, et al. Obstetric management of hepatitis C-positive mothers: analysis of vertical transmission in 559 mother-infant pairs. *Am J Obstet Gynecol*. 2008;199(3):315 e311-315. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18771997>.
  45. Bal A, Petrova A. Single clinical practice's report of testing initiation, antibody clearance, and transmission of hepatitis C virus (HCV) in infants of chronically HCV-infected mothers. *Open Forum Infect Dis*. 2016;3(1):ofw021. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26985444>.
  46. Polywka S, Pembrey L, Tovo PA, Newell ML. Accuracy of HCV-RNA PCR tests for diagnosis or exclusion of vertically acquired HCV infection. *J Med Virol*. 2006;78(2):305-310. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16372293>.
  47. Kuncio DE, Newbern EC, Johnson CC, Viner KM. Failure to test and identify perinatally infected children born to hepatitis C virus-infected women. *Clin Infect Dis*. 2016;62(8):980-985. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26797211>.
  48. Watts T, Stockman L, Martin J, Guilfoyle S, Vergeront JM. Increased risk for mother-to-infant transmission of hepatitis C virus among medicaid recipients - Wisconsin, 2011-2015. *MMWR Morb Mortal Wkly Rep*. 2017;66(42):1136-1139. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29072864>.
  49. Towers CV, Fortner KB. Infant follow-up postdelivery from a hepatitis C viral load positive mother. *J Matern Fetal Neonatal Med*. 2019;32(19):3303-3305. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29587561>.